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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

FERNANDEZ, SUSAN EMILY

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 04/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/784,980

Applicant(s)

SAVRASOVA ET AL.

Examiner

Susan E. Fernandez

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 12/22/04, 7/9/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

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DETAILED ACTION

Claims 1-13 are pending and are presented for examination.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 10, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Tsuchida et al. (JP 360047692).

Tsuchida et al. teaches the cultivation of three strains of *Escherichia coli* for the production of L-threonine in high yield. Because there is a high yield of L-threonine, the bacterium has enhanced expression of genes for L-threonine biosynthesis. The culture medium contains xylose and glucose. See translated abstract.

A holding of anticipation is clearly required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuchida et al. in view of Nichols et al. (Applied Microbiol Biotechnol, 2001, 56: 120-125) or Aristidou et al. (Current Opinion in Biotechnology, 2000, 11: 187-198).

Tsuchida et al. teaches the cultivation of three strains of *Escherichia coli* for the production of L-threonine in high yield. Because there is a high yield of L-threonine, the bacterium has enhanced expression of genes for L-threonine biosynthesis. The culture medium contains xylose and glucose. See translated abstract.

Tsuchida et al. does not expressly disclose a culture medium containing arabinose in addition to xylose and glucose, or that the mixture of sugars is a feedstock mixture of sugars obtained from cellulosic biomass. Furthermore, it does not teach using a bacterium modified for increased rate of pentose sugar utilization.

Nichols et al. and Aristidou et al. teach the construction of *E. coli* strains which grow in hemicellulose hydrosylates and produce ethanol. See the abstract, and first two paragraphs under "Discussion" on page 124 of Nichols et al., and the "Escherichia coli" section on pages 190 and

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191 of Aristidou et al. Furthermore, the cellulosic biomasses for *E. coli* cultivation comprise of glucose, arabinose, and xylose (page 124, first paragraph under “Discussion” of Nichols et al., page 190, first paragraph under “Escherichia coli” of Aristidou). Moreover, Nichols et al. and Aristidou et al. both teach the use of *E. coli* strains engineered for enhanced pentose sugars utilization. In particular, Nichols et al. constructed the *ptsG* mutant FBR14 which ferments arabinose and xylose simultaneously with glucose; unlike parent strain FBR5 (page 124, third paragraph under “Discussion”). Aristidou et al. discusses a recombinant strain of *E. coli* capable of fermenting glucose first, then arabinose and xylose (page 190, second column, first full paragraph).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have used the cellulosic biomass as discussed in Nichols et al. and Aristidou et al. as the culture media for practicing the Tsuchida invention. Furthermore, it would have been obvious to have engineered the *E. coli* strains of the Tsuchida invention for increased rate of pentose sugars utilization.

One of ordinary skill in the art would have been motivated to do this because the use of abundant renewable resources such as cellulosic biomass for ethanol production is highly desirable. Aristidou states that “ethanol is a versatile transportation fuel that offers high octane, high heat of vaporization, and other characteristics that allow it to achieve higher efficiency use in optimized engines than gasoline” (page 188, first column, first full paragraph). Thus the production of ethanol in addition to amino acids would have been desired, and cellulosic biomass would have served as a less expensive alternative to other sources of sugars. Additionally, modifying the bacterium in order to increase the rate of pentose sugars utilization would have

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increased the yield of amino acids from pentose sugars, thus optimizing the process. A holding of obviousness is therefore proper.

Claims 1-5 and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols et al. in view of Hashiguchi et al. (US Pat. 5,998,178).

Nichols et al. discloses the growth of *E. coli* strains in hemicellulose hydrosylates in order to produce ethanol. See the abstract, and first two paragraphs under "Discussion" on page 124 of Nichols et al. Furthermore, the cellulosic biomass for *E. coli* cultivation comprises of glucose, arabinose, and xylose (page 124, first paragraph under "Discussion" of Nichols et al.). Moreover, Nichols et al. teaches the use of *E. coli* strains engineered for enhanced use of pentose sugars utilization. Various strains were examined, including W3110 (Table 1, page 121). The W3110 strain was transformed with the *pet* plasmid, pLOI297, which resulted in increased utilization of xylose when grown in media consisting of xylose and glucose (page 122, first column, first full paragraph, and Fig. 1a, b). Furthermore, a *ptsG* mutant FBR14 was constructed which ferments arabinose and xylose simultaneously with glucose, unlike parent strain FBR5 (page 124, third paragraph under "Discussion").

Nichols et al. does not expressly disclose the production of L-isoleucine.

Hashiguchi et al. discloses preparing an L-isoleucine-producing bacterium. Furthermore, Hashiguchi et al. notes that "L-isoleucine can be prepared in good efficiency by cultivating a bacterium belonging to the genus *Escherichia* which is transformed by incorporating the released type thrABC operon prepared above and which further carries the released type ilvGMEDA operon in a suitable medium to thus produce L-isoleucine and accumulate it in the culture

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medium” (column 23, lines 51-58). *E. coli* W3110 strain is included as an example (column 16, lines 61-66).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have transformed the W3110 strain discussed in Nichols et al. in the same manner as disclosed in Hashiguchi et al. in order to yield L-isoleucine.

One of ordinary skill in the art would have been motivated to do this because Hashiguchi et al. states that L-isoleucine is “essential for human and other animals and is principally useful as a material for various drugs represented by a medicine for promoting nutrition (nutrient)” (column 1, lines 8-11). It would have been obvious to have enhanced isoleucine production in ethanol-producing *E. coli*. A holding of obviousness is therefore proper.

Claims 1-5, and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deabov et al. (RU 2003677C) in view of Nichols et al.

Deabov et al. discloses a strain of *Escherichia coli* capable of producing a higher yield of L-histidine. See DERWENT abstract.

Deabov et al. does not expressly disclose a culture medium for *E. coli* cultivation comprising of arabinose, xylose, and glucose, or that the mixture of sugars in the medium is obtained from cellulosic biomass. Furthermore, the modification of the L-histidine-producing bacterium in order to increase the rate of pentose sugars utilization is not disclosed.

Nichols et al. discloses the growth of *E. coli* strains in hemicellulose hydrosylates in order to produce ethanol. See the abstract, and first two paragraphs under “Discussion” on page 124 of Nichols et al. Furthermore, the cellulosic biomass for *E. coli* cultivation comprises of

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glucose, arabinose, and xylose (page 124, first paragraph under "Discussion" of Nichols et al.). Moreover, Nichols et al. teaches the use of *E. coli* strains engineered for enhanced use of pentose sugars utilization. Various strains were examined, including W3110 (Table 1, page 121). The W3110 strain was transformed with the *pet* plasmid, pLOI297, which resulted in increased utilization of xylose when grown in media consisting of xylose and glucose (page 122, first column, first full paragraph, and Fig. 1a, b). Furthermore, a *ptsG* mutant FBR14 was constructed which ferments arabinose and xylose simultaneously with glucose, unlike parent strain FBR5 (page 124, third paragraph under "Discussion").

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have used the cellulosic biomass as discussed in Nichols et al. as the culture media for practicing the Debabov invention. Furthermore, it would have been obvious to have engineered the *E. coli* strains of the Debabov invention for increased rate of pentose sugars utilization.

One of ordinary skill in the art would have been motivated to do this because the use of abundant renewable resources such as cellulosic biomass for ethanol production is highly desirable. Ethanol can be used as an efficient fuel for automobiles. Thus the production of ethanol in addition to amino acids would have been desired, and cellulosic biomass would have served as a less expensive alternative to other sources of sugars. Additionally, modifying the bacterium in order to increase the rate of pentose sugars utilization would have increased yield of amino acids from pentose sugars, thus optimizing the process. A holding of obviousness is therefore proper.

Claims 1-5 and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols et al. in view of Liaw et al. (US 2002/0106800).

Nichols et al. the growth of *E. coli* strains in hemicellulose hydrosylates in order to produce ethanol. See the abstract, and first two paragraphs under "Discussion" on page 124 of Nichols et al. Furthermore, the cellulosic biomass for *E. coli* cultivation comprises of glucose, arabinose, and xylose (page 124, first paragraph under "Discussion" of Nichols et al.). Moreover, Nichols et al. teaches the use of *E. coli* strains engineered for enhanced pentose sugars utilization. Various strains were examined, including W3110 (Table 1, page 121). The W3110 strain was transformed with the *pet* plasmid, pLOI297, which resulted in increased utilization of xylose when grown in media consisting of xylose and glucose (page 122, first column, first full paragraph, and Fig. 1a, b). Furthermore, a *ptsG* mutant FBR14 was constructed which ferments arabinose and xylose simultaneously with glucose, unlike parent strain FBR5 (page 124, third paragraph under "Discussion").

Nichols et al. does not expressly disclose the production of L-threonine.

Liaw et al. discloses the preparation of *E. coli* ADM Kat26, which is obtained by infecting *E. coli* W3110 strain with a P1 lysate. See page 17, paragraph 0237. This strain is capable of producing threonine.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have infected the W3110 strain discussed in Nichols et al. with the P1 lysate of Liaw et al. in order to allow for threonine production.

One of ordinary skill in the art would have been motivated to do this because amino acids such as threonine may be used in food additives and medicines. It would have been obvious to

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have enhanced threonine production in ethanol-producing *E. coli*. A holding of obviousness is therefore proper.

Claims 1-5, and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dunkak et al. (US Pat. 5,939,295) in view of Nichols et al.

Dunkak et al. discloses a strain of *Escherichia coli* capable of producing tryptophan. See claims 1-11 and the abstract.

Dunkak et al. does not expressly disclose a culture medium for *E. coli* cultivation comprising of arabinose, xylose, and glucose, or that the mixture of sugars in the medium is obtained from cellulosic biomass. Furthermore, the modification of the L-tryptophan-producing bacterium in order to increase the rate of pentose sugars utilization is not disclosed.

Nichols et al. discloses the growth of *E. coli* strains in hemicellulose hydrosylates in order to produce ethanol. See the abstract, and first two paragraphs under "Discussion" on page 124 of Nichols et al. Furthermore, the cellulosic biomass for *E. coli* cultivation comprises of glucose, arabinose, and xylose (page 124, first paragraph under "Discussion" of Nichols et al.). Moreover, Nichols et al. teaches the use of *E. coli* strains engineered for enhanced pentose sugars utilization. Various strains were examined, including W3110 (Table 1, page 121). The W3110 strain was transformed with the *pet* plasmid, pLOI297, which resulted in increased utilization of xylose when grown in media consisting of xylose and glucose (page 122, first column, first full paragraph, and Fig. 1a, b). Furthermore, a *ptsG* mutant FBR14 was constructed which ferments arabinose and xylose simultaneously with glucose, unlike parent strain FBR5 (page 124, third paragraph under "Discussion").

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At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have used the cellulosic biomass as discussed in Nichols et al. as the culture media for practicing the Dunkak invention. Furthermore, it would have been obvious to have engineered the *E.coli* strains of the Dunkak invention for increased rate of pentose sugars utilization.

One of ordinary skill in the art would have been motivated to do this because the use of abundant renewable resources such as cellulosic biomass for ethanol production is highly desirable. Ethanol can be used as an efficient fuel for automobiles. Thus the production of ethanol in addition to amino acids would have been desired, and cellulosic biomass would have served as a less expensive alternative to other sources of sugars. Additionally, modifying the bacterium in order to increase the rate of pentose sugars utilization would have increased yield of amino acids from pentose sugars, thus optimizing the process. A holding of obviousness is therefore proper.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan E. Fernandez
Art Unit 1651
Assistant Examiner

sef



FRANCISCO PRATS
PRIMARY EXAMINER